c.) Remarks

The claims are amended in order to recite the present invention with the specificity required by statute. No new matter is added.

In parent application No. 09/496,041, claims 1-8 and 20 were objected to, or rejected under 35 U.S.C. 112, first and/or second paragraphs, for lack of enablement or as being indefinite. These points are addressed by the foregoing amendment.

The specification was previously objected to; the Examiner stated SEQ ID NOS: 1-4 were not referred to therein. In response, SEQ ID NOS: 1 and 2 are discussed at page 24, lines 35 et. seq., and SEQ ID NOS: 3 and 4 are discussed at page 29, lines 10 et. seq.

Claims 1, 2, 5 and 7 were rejected under 35 U.S.C. 102(b) as being anticipated by Fujio et al. Previously, the Examiner stated the language "to accumulate said precursor of the purine nucleotide in the culture" does not require cell membrane permeability to "secrete" XMP outside the cell. Accordingly, since Fujio teaches XMP production within the cell, the Examiner argues such is "in the culture." For that reason, in order to squarely overcome this rejection, claim 1 is above amended to recite to accumulate said precursor of the purine nucleotide "in the culture medium".

The Examiner also argued that Fujio teaches adding Nymeen S-215 and xylene to culture broth for promoting cell membrane permeability to nucleotides. To the extent the Examiner contends Fujio thus relates to secreting XMP, such is respectfully traversed.

As the Examiner is aware, the present invention is characterized by culturing a recombinant microorganism transformed with a gene which can express an enzyme capable of converting a precursor (for example, guanosine) to purine nucleotide (for example, GMP). The host microorganism has the ability to produce the precursor.

After accumulation of the precursor in the culture medium, the precursor is converted to the purine nucleotide by inducing gene expression in the host.

That is, according to the language of the present claims, fermentation to produce a precursor of the nucleotide and the reaction to convert said precursor into the nucleotide can, if desired, be carried out (i) separately and (ii) successively using only one microorganism in one fermentor. Accordingly, there is no feedback inhibition of precursor production by the produced nucleotide.

Fujio does not explicitly or inherently teach this process.

Fujio relates to producing GMP using E. coli transformed with a GMP synthetase gene. In Fujio, the E. coli transformant is cultured (in the absence of a substance promoting cell membrane permeability such as Nymeen). After culturing, GMP synthetase expressed ion is induced in the E. coli. Thereafter *Corynebacterium ammoniagenes* culture containing XMP is admixed with the E. coli culture in the presence of Nymeen, so as to produce GMP.

Obviously the Fujio process differs in kind from the process of the present invention.

Claims 1 and 3-6 were also rejected under 35 U.S.C. 102(b) as anticipated by Usuda et al. In response, claim 1 is amended to recite that the DNA comprises "an expression-inducible promoter" so as to clarify that expression of the enzyme capable of synthesizing the purine nucleotide from the precursor is induced by use of the expression inducible promoter. The subject matter of this amendment is found at specification page 13, lines 5-12 and from page 14, line 30 to page 14, line 11.

At the very least, Usuda does not teach or suggest producing nucleotides using an expression inducible promoter .

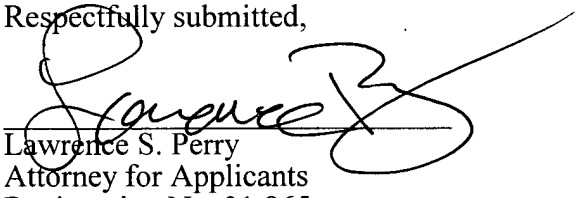
In any event, as to Usuda, the Examiner previously stated that such does not teach away from accumulating purine nucleotides (due to feedback inhibition by GMP) because use of Nymeen S-215 in culture provides permeability of cell membranes to nucleotides. While such contention is mooted by the above amendment, Applicants respectfully wish to clarify the record as follows.

It is common knowledge to those skilled in the art that XMP formation in E. coli is inhibited by a trace amount of GMP in the cell. While Nymeen raises cell membrane permeability, even if Nymeen is used in combination with Usuda, the concentration of GMP in the cell is not reduced to zero. At the very least, GMP remains in the cell at the same concentration as in the culture medium. Therefore, even though Nymeen allows nucleotides to pass through cell membranes, the problem of feedback inhibition is not resolved.

Claims 1, 3-8, 20 and 21 are presented.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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